REMARKS

Reconsideration and allowance are respectfully requested. New claims 96-101 and 106-111 are directed to the elected invention.

Claims 96-115 are pending. Non-elected claims 23-24, 26-28 and 95 were withdrawn from consideration by the Examiner. Applicants cancel the non-elected claims without prejudice to future prosecution of that subject matter. With regard to the possibility that the kit claims will be withdrawn from consideration as directed to a non-elected invention, Applicants request their rejoiner when the elected method claims are allowed. The method and the kit used to practice the method clearly have unity of invention.

The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry.

Specification/Claim Objections

The specification was objected to by the Examiner as allegedly informal. In accordance with her requirement, sequence identifiers are inserted.

Withdrawal of the objection is requested.

35 U.S.C. 112 – Definiteness

Claims 1-19 were rejected as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse.

Most of the objection raised by the Examiner are mooted by the present claim amendments. The exception is "analog" as applied to a whole ESAT-6 antigen or a peptide epitope derived from ESAT-6. In the claims, such analogs are specified to be recognized by T cells responsive to the whole ESAT-6 antigen or the peptide epitope derived therefrom. Derivation of the peptide epitope(s) from ESAT-6 shows that they are a subsequence of SEQ ID NO: 36 (i.e., shorter). This relationship is reinforced by the examples provided in SEQ ID NOS: 1 to 17.

The term "analog" is clear and definite in the context of the present claims.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 112 – Enablement

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 1-19 were rejected as allegedly "failing to comply with the enablement requirement." Applicants traverse.

The Examiner on page 10 of the Office Action suggested that "[t]he claims should be limited to diagnosing in an individual recent exposure to *M. tuberculosis*." As she acknowledges, the use of ESAT-6 is supported by working examples and would allow distinguishing between patients with tuberculosis and those who have been vaccinated with BCG. Applicants disagree, however, with the Examiner's allegation on page 11 of the Office Action that only peptide epitopes of SEQ ID NOS: 1 to 17 are enabled. The latter are merely exemplary. The entire amino acid sequence of ESAT-6 is known and described in the present specification. Making and using peptide epitopes from ESAT-6 would not require experimentation because specifying a subsequence of SEQ ID NO: 36 and synthesizing it is well known in the art. The newly synthesized peptide epitope could be assayed for T-cell responsiveness for any length from a few residues to larger (e.g., 8 to 29 amino acids in length).

Analogs are enabled by Applicants' teachings in their specification and general knowledge in the art. First, claims 96 and 106 contain a functional definition of the term "analog" based on the responsiveness of T cells to whole ESAT-6 antigen and peptide epitopes derived therefrom. The analogs would have to induce a response by the same T cells. Since the process of T-cell recognition is well understood, the structure of the analog must be related to the structure of the whole ESAT-6 antigen or peptide epitope recognized by the T cell's receptor. Thus, the function and structure are shared between the "analog" and the whole ESAT-5 antigen or peptide epitope. Second, as of the filing

date of this application, methods were known to those skilled in the art for the prediction of a peptide epitope (i.e., subsequences) within full-length amino acid sequences of a native antigen that might also be applied to analogs of the peptide epitopes recognized by T cells. For example, Meister et al. ("Two novel T cell epitope prediction algorithms based on MHC-binding motifs: Comparison of predicted and published epitopes from Mtb and HIV protein sequences" Vaccine 13:581-591, 1995), see also WO 01/70774, and Panigada et al. ("Identification of a promiscuous T-cell epitope in *Mycobacterium tuberculosis* Mce proteins" Infect. Immun. 70:79-85, 2002) which are attached. Using such algorithms, candidate peptides can be identified, synthesized, and confirmed as equivalent to whole ESAT-6 antigen or peptide epitope by ELISPOT assay. Copies of WO 01/70774 and Panigada are attached for the Examiner's consideration.

Withdrawal of the enablement rejection made under Section 112, first paragraph, is requested because it would not require undue experimentation for a person of skill in the art to make and use the claimed invention.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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